

Factors That May Predict Sexuality Changes in Men with Newly-Diagnosed Acute

Leukemia Cancer: Fatigue, Pain, Distress

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Background

Acute leukemia is a harsh diagnosis that requires intense treatment to achieve and maintain remission (Ferrara, Schiffer, 2013; Fleming, 2013). A new diagnosis of acute leukemia can bring about life altering changes that affect the patient and persons close to them (Beavers, Lester). The care and treatment for acute leukemia patients spans over years including interventions for symptoms caused by both the cancer and treatment (Beavers, Lester). Patients may experience distress with treatment decisions and each chemotherapy cycle (Beavers, Lester). With each stage of treatment, the lifestyle of men can change due to significant side effects of the cancer diagnosis and treatment.

A holistic approach may enhance psychosocial and physical care and provide for individualized interventions. Experienced psychosocial problems are understudied and often overlooked in acute leukemia survivors (Allart, Soubeyran, Cousson-Gelie, 2013; Danhauer et al., 2013; Rodin et al., 2013). Management of psychological and physical distress is essential to avoid alterations in quality of life (Kent, Mitchell, Oakley-Girban, Arora, 2014; Kent, Mitchell, Oakley-Girban, Arora, 2014). Examination of needs may improve survivorship care. Men with acute leukemia may report a number of distressing issues, including fatigue, pain, and sexuality.

Conceptual Framework

Our study framework and analyses are based on the Lenz theory of unpleasant symptoms. Lenz et al (2008) explain that the theory of unpleasant symptoms has three main components, which include the symptoms that the patient experiences, the influencing factors that cause or have an effect on attributes of the symptom experience, and the outcomes associated with the symptom experience (Lenz, Pugh, 2008). The symptoms are central to the theory with presumed commonalities across different symptoms that may be experienced by clinical populations in a

variety of situations (Lenz, Pugh, 2008). Application of this theory to the symptoms experienced by men with acute leukemia illustrates the potential physiologic, psychologic, and situational factors that may lead to the group of self-reported symptoms of distress, fatigue with an observed effect on performance secondary to sexuality changes in newly-diagnosed acute male leukemia survivors.

Distress

Acute leukemia can induce lifestyle changes that affect levels of distress. Patients are undergoing social setting changes, new treatment regimens, body changes, and more that can contribute to an increase in distressing psychosocial or physical issues. Side effects are persistent with complications from pre-existing comorbid health conditions, elevated distress, decreased social support, functional impairments, and significant fatigue (Petty, Lester, 2014). Predictors of post-traumatic distress have been identified in persons with acute leukemia (Rodin, et al., 2013). Previously we studied groups of acute leukemia survivors (N=100) at time points of active treatment (induction therapy), end of treatment, and 3 and 6 months later self-reported elevated distress levels using the distress thermometer. There were no significant group differences ($P=0.18$) indicating that distress is ubiquitously present in early survivorship. ($M_s=3.6-5.0$; Lester, et al., *in press*). In newly-diagnosed or relapsed adult leukemia survivors (N=249), patients reported a median of two psychological and nine physical symptoms (16). In a study that examined gender differences, men were found to be passive without expression of emotional issues, although desire more medical information than women (20).

Fatigue

Fatigue is the most common symptom expressed by cancer survivors, including patients with acute leukemia (Lester, et al., *in press*). Side effects of cancer treatment persist with complaints of significant fatigue (Petty, Lester, 2014). Newly-diagnosed or relapsed adult leukemia survivors also reported a persistent lack of energy. Leukemia patients find chronic fatigue to be more distressing and disabling than other cancer-related symptoms, including pain, depression and nausea. The fatigue can begin before cancer is even diagnosed; in fact, fatigue may be a primary symptom that sends persons to their primary care provider. Fatigue can worsens during treatment and may persist for months, even year following the end of treatment (Leukemia and Lymphoma Society, nd). Persons with acute or chronic fatigue report a level of exhaustion that is not overcome with sleep or rest (Leukemia and Lymphoma Society, nd). In our study of newly-diagnosed acute leukemia patients at various time points as described above, survivors self-reported physical symptoms using the distress thermometer problem list. Fatigue was self-reported as the highest physical symptoms (63%). Fatigue is a common problem in persons with acute myelogenous leukemia, even when controlling for the effects of anemia (Cheng, Hourigan, Smith, 2014)

Pain

Pain is a subjective symptom that patients with acute leukemia can experience from pre-diagnosis through permanent survivorship. Pain is a common presenting symptom prior to diagnosis (Davis, Viera, Mead, 2014). Physical changes, diagnostic testing, and treatment can all contribute to patients' pain perception. The disease itself can cause bone or joint pain due to overcrowding in the bone marrow by cancer cells (Leukemia and Lymphoma Society, nd). The

cancer cells may form a mass near the spinal cord's nerves or in the joints. The bone pain is most often perceived in the long bones of the arms, legs, ribs, and sternum. The excess of cells may cause joint pain and swelling in the hips and shoulders. In acute lymphocytic leukemia, bone pain is reported in 25 percent of patients at the disease's onset, although bone pain is less common in patients with acute myeloid leukemia (Leukemia and Lymphoma Society, nd)

Sexuality

Sexuality is a common topic of concern for cancer patients, although one that is frequently not discussed. In a study of patients treated for hematologic malignancies, sexuality, sexual desire, and sexual ability decreased one month after treatment which contributed to lower quality of life. (Olsson, Sandin-Bojö, Bjuresäter, Larsson, 2015). Men experience significant changes in sexuality after a cancer diagnosis (Gilbert, Ussher, Perz, Wong, Hobbs, Mason, 2014). Men with various cancer types (N=21) reported erectile dysfunction, decreased libido and desire, and difficulty with orgasm (Gilbert, et al., 2013). Most men were in supportive relationships and accepted sexuality changes, putting them in the context of natural aging (Gilbert et al., 2013). A study of men (n=34) and women (36) post-allogeneic transplant for the treatment of acute and chronic leukemia, participants reported a deterioration of sexual relations (59%) and worsened social relationships (25%) (Claassens, Beerendonk, Schattenberg, 2006). An interest in sex, sexual activity and pleasure from sex deteriorated in nearly 60% of the patients; half of these patients were under age 50 (Claassens, 2006). In this study (Claassens, 2006) men reported pain during sexual intercourse, erectile dysfunction, delayed or no orgasm/ejaculation, or early orgasm/ejaculation. In our first study of acute leukemia patients (N=100) as described above,

alterations in sexuality was reported as one of the top three symptoms of concern and increased distress during early survivorship in participants with acute leukemia.

Purpose

The purpose of our secondary analysis was to examine factors of distress, fatigue, and pain and their effect on sexuality as self-reported by acute leukemia patients during active treatment (induction), end of treatment, and three and six months post treatment.

Methods

Research Design

A longitudinal design with repeated measures was used to measure levels of self-reported distress, fatigue, and pain in male patients newly-diagnosed with acute leukemia and their effect on alterations in sexuality.

Sample

Men (n=82) and women (72) were accrued from November 2013 through February 2015 from the acute leukemia clinics and inpatient units at a freestanding university-based, National Cancer Institute-designed comprehensive cancer center.. The Cancer Institutional Review Board atThe Ohio State University in Columbus, Ohio approved the study. The study sample met inclusion criteria of persons with a recent diagnosis of acute leukemia, age 18 or older, able to provide consent, willing to complete questionnaires every 3-6 months for up to four years after the end of active treatment, able to read, write, and communicate in English, and no significant mental health conditions impairing cognition (e.g. schizophrenia, mental retardation, dementia). The study sample self-reported distress and associated symptoms at noted time points from

diagnosis, active treatment (induction), and three months post end of active treatment. Our secondary analysis is centered on the male sample (N=82). Men completed their self-reported questionnaires at specific time points as designated in the study: at diagnosis, during active treatment/induction, and three months later. The time period designated as diagnosis included the initial diagnosis and the beginning of their induction therapy. Patients that were newly-relapsed were also included in the sample. Outcome measures included the self-reported level and source of distress, intensity of fatigue and interference in daily activities, occurrence, location, and intensity of pain, and sexual functioning.

Measures

Distress thermometer problem list: The Distress Thermometer (DT) was crafted by members of the National Comprehensive Cancer Network (NCCN). It allows the patient to self-report their level and cause of distress (NCCN, 2014). The DT is a brief, self-report instrument that provides screening data about distress related to a cancer diagnosis and its impact on the person's psychological status. The answer options on the 38-item problem list are yes/no to report sources of distress on five subscales: family (4 items), emotional (6 items), physical (21 items), practical (6 items), and spiritual sources (1 item). Items are totaled and provide both subscale and total item scores (0 to 38). At the end of questionnaire, two author-derived free response items were included to allow patients to report any other disease-related issues: "What are your top three causes of distress" and "What are your three most distressing symptoms".

Demographic and caregiver information: The demographic form was comprised of self-report items related to issues about residency, patient (and partner) responsibilities, and information about the caregiver and support system. Additional items provide information about location of residence, level of education, marital status, dependents, age of dependents, and any other

dependent responsibilities such as adult children/grandchildren/elderly parents. In addition, household income before cancer diagnosis, current household income, employment status, previous/current occupation, and health insurance status/type of insurance is reported.

Brief pain inventory: The Brief Pain Inventory (14 items) is a self-report questionnaire designed to assess the occurrence, location, and intensity of pain. The five-item Likert-type scale enables measurement of pain intensity and its response to various interventions. In addition, the seven-item reactive dimension measures the interference of pain in daily life with a 0-10 scale (0 = 'no pain/interference at all, 10 = 'pain as bad as you can imagine/complete interference). A diagram allows patients to mark where on the body the pain is experienced (Tan, Jensen, Thornby, and Shanti, 2004).

Brief fatigue inventory: The Brief Fatigue Inventory measures the severity or intensity of fatigue, and the impact, or interference on daily functioning in patients with cancer. Reliability of the instrument was measured with Cronbach's alpha (0.82 – 0.97; MD Anderson Cancer Center [MDACC], 2012). A global fatigue score can be obtained by examining all completed items to obtain an average score (MDACC, 2012). The Brief Fatigue Inventory was studied in head and neck cancer patients (N=52) as compared to persons without cancer (N=57) to measure the frequency and reported intensity of fatigue (Aynehchi, Obourn, Sundaram, Bentsianov, Rosenfeld, 2013). The Brief Fatigue Inventory has been translated into a number of languages.

Male Urogenital & Sexuality Questionnaire: Information about male sexuality was obtained using a couple instruments including the international index of erectile function (IIEF5), a multidimensional scale for the assessment of erectile function, including treatment-related changes in men with erectile dysfunction (Rosen, et al., 1997). The American Urological

Association symptom index for benign prostatic hyperplasia was used to measure nocturia, frequency, weak urinary stream, hesitancy, intermittence, incomplete emptying, and urgency (Barry, et al., 1992). Four items were added to measure desire and communication.

Data Analyses

Descriptive analyses: Demographic data (categorical and continuous data) were summarized using descriptive statistics such as frequencies and percentages across type of cancer (categorical data), and visit time (categorical data). With consideration to the specific parameter, central tendencies were reported; means and standard deviations were calculated as appropriate.

Primary analyses: Chi square was used to identify relationships between categorical variables and time periods; post hoc tests using Bonferonni were applied to determine significance to specified time periods. Analysis of variance (ANOVA) was used to identify relationships between continuous variables and time periods; post hoc tests using Tukey's were applied to determine significance to specified time periods. Multivariate analysis of variance (MANOVA) was used to examine relationships between specific symptoms, sexuality, and specific time periods. Linear stepwise regression was used to identify symptom predictors of fatigue in the first year of treatment. Each symptom (e.g. distress, fatigue, and pain) were measured to determine significant findings.

Results

The presence or absence of each self-reported symptom was examined for each time period using yes/no response options on respective measurement instruments. We found that the most common time periods of participant self-reporting were at diagnosis (n=82), during active treatment/induction (n=60), and 3-month post treatment (n=49) time points. Eighteen percent of patients (n=15) did not reach time points past induction therapy or three months post treatment due to their demise.

Distress

Male leukemia participants self-reported a mean distress score (Figure 1) of 4.4 (sd = 2.83) on the distress scale with a mean of 10.53 (sd = 6.76) sources of distress. Using tests of Chi-square, significant findings were associated with treatment decisions, and physical symptoms such as fevers, getting around, mouth sores, and sexuality, Post hoc tests on significant categorical and continuous variables indicated that no significant differences existed between various time points ($P=0.9$). Likewise, no significant findings were identified between levels of distress and factors related to male sexuality ($P_s < 0.11$)

Fatigue

Male leukemia participants self-reported the presence of fatigue as a physical symptom on the distress problem list (52%). There were no significant differences between fatigue and specific time periods ($P=0.28$) indicating that the level of fatigue is high and present over time periods. Fatigue was compared to factors of sexuality and sexual function. All factors were significant (Table 1) indicating that fatigue may interfere with all noted factors of sexuality and sexual function ($P_s \leq 0.05$).

Pain

Male leukemia participants self-reported the presence of pain as a physical symptom on the distress problem list (53%). The level of pain significantly decreased over time periods (Figure 2). Significant findings were noted for several factors: satisfaction, penetration, maintenance of erection, and difficulty with maintenance of erection ($P < 0.04$).

Sexuality

Male leukemia participants self-reported issues with several factors related to male sexuality and sexual function (scale 0-100): confidence to achieve and maintain an erection

($M=31.7$, $SD=44.3$), erection hard enough to penetrate ($M=30.5$, $SD=43$), ability to complete intercourse ($M=30.5$, $SD=43$), satisfaction with intercourse ($M=30.7$, $SD=43$), worry of pain in genital area ($M=24.2$, $SD=43.7$), ability to talk with partner about sexual concerns ($M=24.7$, $SD=41$), interest in sexual activity ($M=25.5$, $SD=42$), desire for sexual activity ($M=26.7$, $SD=42.8$), and happy with sex life ($M=25.4$, $SD=42$). The wide variety of participant responses (e.g. wide standard deviation) requires additional research and direct examination of questionnaires.

Significant findings ($P=0.0$) were noted between negative libido or desire and factors related to male sexuality: confidence to achieve and maintain an erection, erection hard enough to penetration, maintenance of erection, difficulty with maintenance, worry about pain in genital area, satisfaction with sex life, ability to talk with partner about sexual concerns, interest in sexual activity, and happy with sex life (Table 3).

Discussion

The identification of distress and symptoms early in the trajectory is important to reduce the likelihood of their continuance in the months to follow. Multiple bodily functions are altered as a result of induction chemotherapy for acute leukemia. Examination of relationships between distress, level of fatigue, libido, and desire for sexuality may identify the overall underlying causes of bothersome issues in sexuality and sexual functioning. It is important for nurses to understand their patients' levels of distress and sources that can evolve with a new diagnosis of cancer, including sexual changes.

Common and pervasive symptoms are present in acute leukemia patients including fatigue, pain, and distress. Upon secondary analysis it was clear there was a correlation between

self-reported sexuality changes in males newly diagnosed with acute leukemia and self-reported elevated fatigue, increased pain, and decreased libido/desire for sexual activity. In males that are struggling with changes in sexuality, we know that factors of pain, fatigue, and libido/desire may all correlate and may cause difficult issues in coping. These findings enable nurses to identify and measure interventions that may enhance sexuality: control of pain, improvements with fatigue, and talking with partner about decreased libido. Prompt discussion of potential changes in sexual function is important in order to avoid yet another alteration in survivors' lives.

Conclusion

Intimacy is an important part of life for most partners, including men with acute leukemia. It is important to talk about pending changes, and what may be done to improve sexual outcomes. Health care providers should be trained to monitor for sign and symptoms of distress. Nurses should facilitate care for acute leukemia patients by providing tools to teach patients how to handle increased levels of distress, fatigue, pain, and decreased libido/desire for sexual activity in a healthy manner. By incorporating these screenings into care, patients can focus on healing by having support and guidance from their medical team to sift through the life tribulations that may occur. Providers often concentrate their care and discussion around medications and treatments. This data indicates health care providers have a responsibility to treat our patients more holistically to meet their needs that are not measured by lab values and tests. Nurses are integral to the care of acute leukemia patients. It is important to include intimacy and sexuality as components of care. Nurses should talk with the patient, significant other, and together as a couple to initiate discussion and potential interventions to avoid complications with pain, fatigue, desire, libido and sexuality.

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Figure 1. Bar chart displaying self-reported level of distress of male participants (N=82).

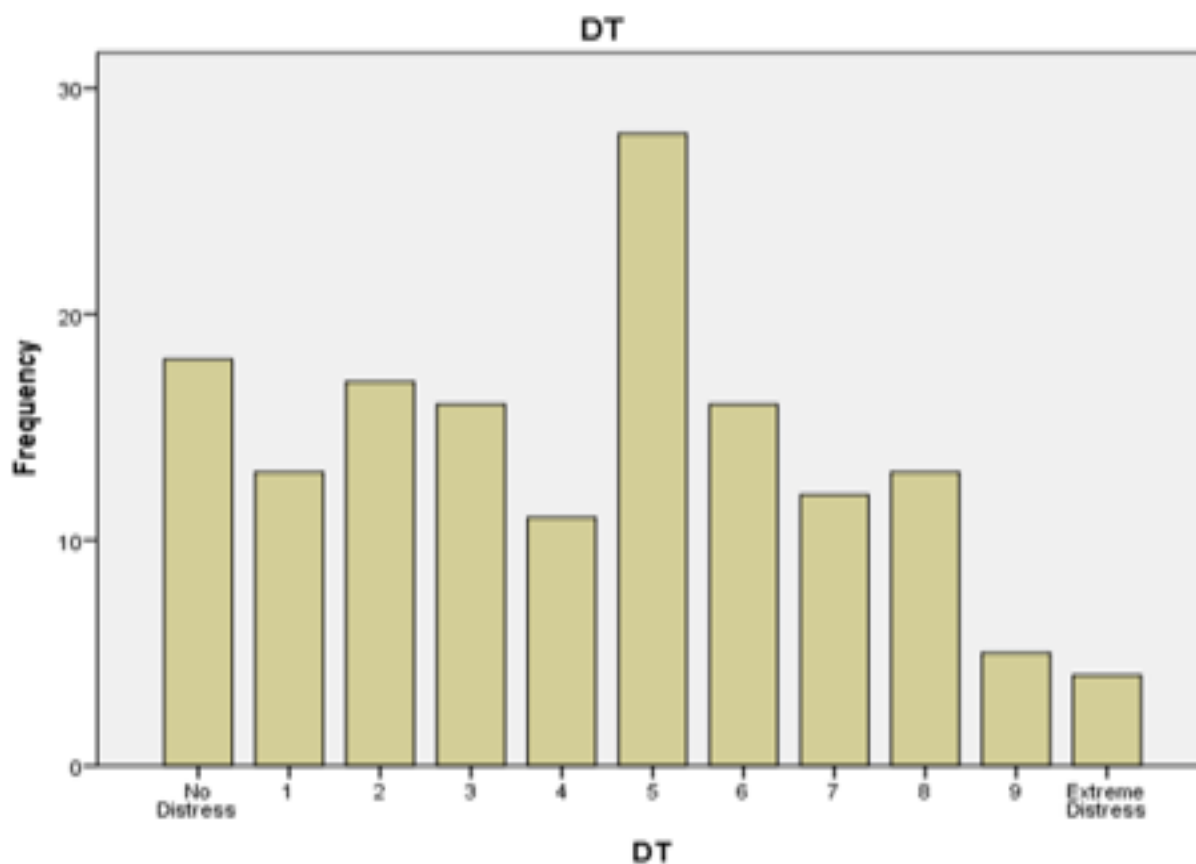


Table 1. Comparison of factors related to sexual performance and the self-reported level of fatigue. Significant findings were noted for all factors.

Factor	<i>P</i> value	Factor	<i>P</i> Value
Confidence	0.0*	Satisfaction	0.0*
Penetration	0.0*	Interest	0.005*
Maintenance	0.0*	Desire	0.01*
Difficulty with Maintenance	0.0*	Happy	0.03*
Worries	0.03*	Talking with Partner	0.05*

$P \leq 0.05$

Figure 2. Bar chart that illustrates a steady decline of the level of pain from diagnosis onward. Specific time periods include 1=diagnosis, 2=active treatment/induction therapy, 3=end of treatment, 4=three months post end of treatment, 5=six months post end of treatment.

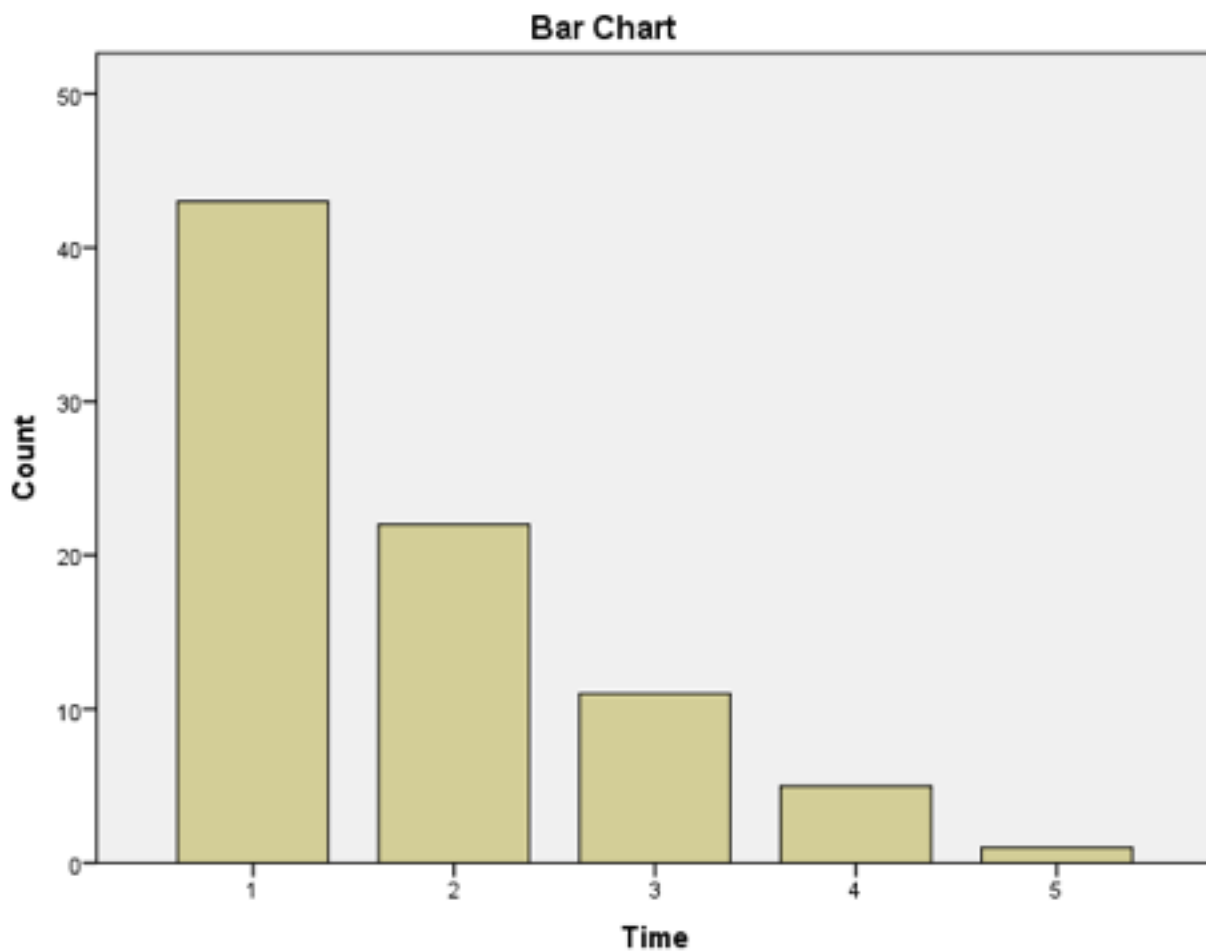


Table 2. . Comparison of factors related to sexual performance and the self-reported level of pain. Significant findings were noted for several factors: satisfaction, penetration, maintenance of erection, and difficulty with maintenance of erection ($P < 0.04$).

	<i>P</i> value	Factor	<i>P</i> Value
Confidence	0.7	Satisfaction	0.04*
Penetration	0.04*	Interest	0.2
Maintenance	0.03*	Desire	0.1
Difficulty with Maintenance	0.03*	Happy	0.2
Worries	0.2	Talking with Partner	0.1

P

Table 3. Display of significant findings ($P=0.0$) between libido or desire and factors related to male sexuality.

Factor	<i>P</i> value	Factor	<i>P</i> Value
Confidence	0.0*	Satisfaction	0.0*
Penetration	0.0*	Interest	0.0*
Maintenance	0.0*	Happy	0.0*
Difficulty with Maintenance	0.0*	Talking with Partner	0.0*
Worries	0.0*		

$P=0.05$